IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Hockersmith
Docket No.: IMET0050
Serial No.: 09/766,427
Examiner: R. Gitomer
Filed: January 18, 2001
Art Unit: 1651
Title: A METHOD OF PRODUCING A GLYCEMIC PROFILE OF PREDETERMINED SHAPE IN A TEST SUBJECT.

DECLARATION OF LINDA J. HOCKERSMITH UNDER 37 CFR §1.132

May 19, 2003

Commissioner of Patents and Trademarks
Washington, DC 20231

Sir:

1. This Declaration is provided in response to the Office Action, dated January 15, 2003, for the above-identified patent application.

2. I am a Registered Dietitian (RD) and a Certified Diabetes Educator (CDE). I consider myself to be a person reasonably skilled in the art to which the claimed invention pertains

3. I respectfully submit that the following would be readily apparent to one having an ordinary level of skill in the art:

a. Dietary carbohydrates are utilized primarily for body fuel;
b. Insulin is a hormone that regulates carbohydrate mechanism;
c. The intestinal system has the ability to breakdown substantially one hundred percent of digestible carbohydrate;

d. The simplest form of carbohydrate is a monosaccharide, *e.g.* glucose;

e. The circulatory system has the ability to transport glucose to all body systems, especially the liver and muscle tissues;

f. Insulin produced by the endocrine system is required to transport glucose into liver and muscle cells;

g. Insulin production and utilization is unlimited in healthy individuals, explaining why indiscriminate carbohydrate intake in non-diabetic individuals results in fasting blood glucose concentration remaining in a relatively constant state between 70 – 126mg/dL.

h. In the diabetic state, blood glucose regulation is compromised; such compromise is the basis of the categorization of different types of diabetes

i. Those having Type 1 diabetes cannot produce insulin due to beta cell demise. Therefore they must take exogenous insulin to maintain life. The dose is often calculated at 1 unit of insulin/kg of bodyweight, and represents approximately 100 percent of their insulin requirement. If exogenous insulin is not administered in the right dose or at the right time, a small amount of carbohydrate will cause blood sugar to move abruptly upwards. There is no endogenous insulin production and only residual insulin from a previous dose would be present to interact with the blood glucose, thus these individuals have a greater sensitivity to carbohydrate challenge;

j. Those having Type 2 diabetes have a mixed problem. Their insulin production may be impaired and their insulin utilization may be resisted. Thus, those having Type 2 diabetes may take exogenous insulin or medication to enhance insulin utilization because of their insulin resistant state. Because the mechanism of insulin utilization is impaired, many Type 2 individuals require >100% of the normal insulin requirement and often have large amounts of insulin in the blood at any one time. Generally, these individuals have a lower sensitivity to a carbohydrate challenge compared to a type I individual;

k. In either case, diabetes treatment is based upon identifying the type of diabetes and administering the proper dose of insulin or insulin-regulating medication to achieve control;

l. Control is defined as a premeal fasting glucose response of 70 – 140 mg/dL or a postprandial reading at approximately 2 hours of greater than 180 mg/dL. It can be measured with each carbohydrate intake, but is usually measured every three months by a glycosylated hemoglobin test (HbA_1C as an average of carbohydrate response;

m. High glycosylated hemoglobin levels are associated with poor control, which can usually be attributed to inadequate medication regimens; and

n. Poor control generally leads to greater sensitivity to carbohydrate challenge.

4. I provide the following additional evidence in support of the above averments:

Exhibit A: L. Krall, R. Beaser, Joslin Diabetes Manual, 12th ed., Lea & Febiger, Philadelphia (1989):

page 2, paragraph 2 in support of item 3a, above;
page 3, paragraph 3 in support of item 3b;
pages 7 – 8 in support of items 3a – g; and
page 16, table 1-1 in support of 3h.

Exhibit B: W. Ganong, Review of Medical Physiology, 19th ed., Appleton & Lange, Stamford CT (1999):

page 318 in support of item 3b, 3e, 3f;
page 325 "Glucose Tolerance" paragraph 1 in support of item 3h;
page 330 "Regulation of Insulin Secretion", paragraph 5 in support of item 3g.

Exhibit C: M Austin, K. Kulkarni, M. Powers, Blood Glucose Monitoring: Essential Skills for Health Care Professionals, Peekytoe Productions, St. Paul MN (2000):

page 4, "What Are the Usual Blood Glucose Goals?", Table 1 – 3 in support of items 3g, 3l;
Page 22, "What is carbohydrate counting?", paragraph 1 in support of item 3c;

Exhibit D: Medical Management of Non-Insulin-Dependent (Type II) Diabetes, 3rd. ed., Clinical Education Series, American Diabetes Association (1994), "Highlights: Pathogenesis":

page 14, in support of item 3j;
page 16, in support of item 3j;

Exhibit E: Medical Management of Non-Insulin-Dependent (Type II) Diabetes, 3rd. ed., Clinical Education Series, American Diabetes Association (1994), "Diabetes Therapeutic Objectives ":

page 26, in support of items 3g, 3l;

Exhibit F: Medical Management of Non-Insulin-Dependent (Type II) Diabetes, 3rd. ed., Clinical Education Series, American Diabetes Association (1994), "Diagnosis and Classification":

page 3 in support of item 3h, 3j;

page 5 in support of item 3j;

Exhibit G: Diabetes Management Therapies: A CORE Curriculum for Diabetes Education, 4th ed., M. Franz, editor, American Association of Diabetes Educators (2001):

page 11 in support of item 3d;
page 13 in support of item 3c;
page 91 in support of item 3k;
page 92 in support of item 3f;
page 103 in support of item 3i;
page 159 in support of items 3l, 3m.

5. I also respectfully submit the following:

a. that blood glucose concentration is nearly universally expressed in mg/dL, or alternately mM, and that this would be readily apparent to the practitioner having an ordinary level of skill;

b. that methods for making invasive blood glucose determinations are widely known, and would be apparent to the practitioner having an ordinary level of skill without further explanation;

c. that the ordinary level of skill in this art is high, wherein a practitioner having an ordinary level of skill would have at least a bachelor's degree, several years work experience and substantial post-graduate training;

d. that the practitioner having an ordinary level of skill would appreciate the application of the invention to a cross-section of subjects without detailed explanation, given the high level of skill in the art;

e. that the invention does not rely on such parameters such as glycemic load and glycemic index for its utility;

f. that exogenous insulin has been in use since the early 20th century, and that there exists a substantial body of knowledge relating to its use; that one having an ordinary level of skill would readily be able to devise a more aggressive dosing regimen with a minimum of experimentation, given the present level of knowledge available and the high level skill in the art.

6. In the above-identified Office Action, the Examiner has stated:

"How X is calculated is critical or essential to the practice of the invention, but not included in the claim(s), nor is it set forth in the specification."

7. Claims 1 and 24 have been amended to described X as an assigned value, thus it is not calculated. In the above-identified patent application, I have taught:

"The formula used to calculate the amount of carbohydrate required to produce that desired glucose excursion is:

$$CHO = \frac{TARGET - STARTING}{X};$$

where CHO is the amount of carbohydrate in grams, Target is the glucose level to be achieved, Starting is the current glucose level and X is a numerical index of the subject's sensitivity to carbohydrate challenge, described in greater detail below" (page 10, line 2 to line 10, emphasis added);

and:

"X is a factor that serves as an index to carbohydrate sensitivity. The initial value is assigned by the clinician, according to type of diabetes and level of diabetes control, from a range of approximately 1 to 3, and is subsequently individualized to the subject." (page 13, line 22 to line 25, emphasis added).

As explained, *supra*, it would be readily apparent to one having an ordinary level of skill, based on the knowledge generally available in the art, as described by the above, and further based on the data provided by tables 1 and 4 of the application would understand that type 2 diabetics, such as subjects 1 – 3, 5 – 7 and 9 – 10, having a relatively lower sensitivity to carbohydrate would be assigned a relatively lower value of X, 1 for example. Type 2 diabetics, such as subject 4 will have a relatively higher sensitivity to carbohydrate challenge, and would be assigned a higher value of X, 2 for example. The subject's HbA_1c value constitutes an additional factor that affects carbohydrate sensitivity. Thus, for example, a type 1 diabetic having a high value for HbA_1c, such as subject 8, would have an even greater sensitivity to carbohydrate challenge, and would therefore be assigned a value of 3, for example.

8. The Examiner has stated:

"How X is calculated is not described in such a fashion as to enable one of skill in this art to perform the calculation." As I have previously described, X is an assigned value, it is not calculated.

9. The Examiner has stated:

"A description of X and X_i is provided in general terms insufficient to be reproduced."

10. I have taught:

"Blood glucose values are measured until the subject's blood glucose values reach a maximum. The actual maximum and the target maximum are compared and an individualized value of X, X_i is calculated according to:

$$X_i = \frac{OBSERVED - STARTING}{CHO},$$

where '***OBSERVED***' represents the observed maximum, as contrasted with the target maximum"(page 13, line 29 to page 14, line 3.) '***STARTING***' and '***CHO***' were previously defined. Thus, one skilled in the art would readily understand that X_i is easily calculated by dividing the difference between starting value and the observed maximum by the amount of carbohydrate given, as calculated in expression 1.

11. The Examiner has stated:

"It is the Examiner's position that one cannot make a calculation based upon the formula in claim 1 because what the required amount of carbohydrate cannot be calculated based on no units of glucose over X, which could be anything."

12. The expression

$$CHO = \frac{TARGET - STARTING}{X}$$

has not been described as an equation or a mathematical expression. Rather, it has been presented as a formula, a "method allowing little room for originality." Collegiate Dictionary, 10th ed. Merriam-Webster (1998). Thus, the formula summarizes simple steps to be followed in determining an amount of carbohydrate. While some of the steps involve calculation, it is unnecessary that the formula reduces or balances because it is not a mathematical expression. Applicant notes that the specification, at page 10, line 2 to page 14, line 15 provides a detailed description of a working example employing the expression and the use of X to determine the required amount of carbohydrate. What is more, I have explicitly taught that the value resulting from following the above steps is to be expressed as grams of carbohydrate (page 10, line 7).

13. The Examiner has stated:

"What the spectroscopic instrumentation based on idealized anti-correlated glycemic profiles may be and how such profiles may then be used to make a model is not set forth in the Claim." One skilled in the art of noninvasive blood glucose determination would readily comprehend the required instrumentation and the generation of an appropriate calibration model, given the teaching of page 5, line 30 to page 6, line 26.

14. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

Respectfully Submitted,

Linda J. Hockersmith 5/19/2003

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